

BIOGRAPHICAL SKETCH

NAME

Jin, Victor Xinhua

eRA COMMONS USER NAME (credential, e.g., agency login)

victorjin

POSITION TITLE

Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Fudan University, Shanghai, China	B.S.	07/88	General Chemistry
Queen's University, Ontario, Canada	Ph.D.	05/01	Biological Chemistry
University of Ottawa, Ontario, Canada	M.S.	04/03	Computer Science
The Ohio State University	Postdoc	11/05	Computational Biology
University of California, Davis	Postdoc	12/07	Genomics/Bioinformatics

A. Personal Statement

Dr. Victor Jin was trained in biological chemistry, epi-/genomics and computational biology. He has authored and co-authored more than 85 peer-reviewed articles, reviews and book chapters, some of which were published in high impact journals. He has been working in the fields of computational biology and functional genomics more than 15 years. In particular, he and his collaborators have pioneered various state-of-art ChIP-based sequencing techniques and novel computational algorithms in cancer cells and tumor tissue samples such as ChIP-seq, MBDCap-seq, ChIP-ePENS and 3C-seq. The current research in his lab includes: 1) developing computational approaches for the identification of genomic regulatory elements and networks from the cancer epi-genomic and genomic regulatory data generated from next generation sequencing (NGS) technologies such as ChIP-ePENS, ChIP-seq, MBDCap-seq, DRIP-seq, TCC (Hi-C), RNA-seq and miRNA-seq; 2) functionally and mechanistically characterizing the computational predictions and providing the meaningful biological interpretations using novel techniques such as siRNA, 3C/ChIP/RT-qPCR, Western Blotting, 3D-FISH and CRISPR/Cas9; and 3) developing computational pipelines to aid molecular biomarker discovery and examining the significance of identified gene signatures in patients' survival and prognostic information.

- a. **Jin VX**, Rabinovich A, Squazzo SL, Green R, Farnham PJ. A computational genomics approach to identify cis-regulatory modules for chromatin immunoprecipitation microarray data – a case study using E2F1 in cancers. *Genome Res* 16:1585-1595, 2006. PMCID: PMC1665642.
- b. Lan X, Witt H, Katsumura K, Ye Z, Wang Q, Bresnick EH, Farnham PJ* and **Jin VX***. Integration of Hi-C and ChIP-seq data reveals the distinct types of transcriptional chromatin linkages. *Nucleic Acids Res* 40:7690-7704, 2012. PMCID: PMC3439894.
- c. Hsu PY, Hsu HK, Lan X, Juan L, Yan P, Labanowska J, Heerema N, Hsiao TH, Chiu YC, Chen Y, Liu Y, Li L, Li R, Thompson, IM, Nephew KP, Sharp ZD, Kirma NB, **Jin VX**, and Huang TH. Amplification of distant estrogen response elements deregulates target genes associated with tamoxifen resistance in breast cancer. *Cancer Cell* 24:197-212, 2013. PMCID: PMC3890247.
- d. Ye Z, Chen Z, Sunkel B, Fietze S, Huang TH, Wang Q*, **Jin VX***. Genome-wide analysis reveals positional-nucleosome-oriented binding pattern of pioneer factor FOXA1. *Nucleic Acids Res* 44:7540-7554, 2016. PMCID: PMC5027512.

B. Positions and Honors

Positions and Employment

1988-1995	Research Scientist, Division of Biochemistry, Shanghai Institute of Pharmaceutical Industry, Shanghai, China
1995-1997	Research Assistant, Department of Chemistry, National University of Singapore, Singapore
2001-2002	Software Engineer, TouchLink, Incorporated, Ottawa, Canada

2003-2005	Post-doctoral Fellow, Human Cancer Genetics, The Comprehensive Cancer Center, The Ohio State University, Columbus, OH
2005-2007	Post-doctor Research Scientist, Genome Center, University of California, Davis, CA
2008-2009	Assistant Professor, Bioinformatics Program, Department of Biology, University of Memphis, Memphis, TN
2009-2013	Assistant Professor, Department of Biomedical Informatics, The Ohio State University, Columbus, OH
2013-present	Associate Professor, Departments of Molecular Medicine and Epidemiology/Biostatistics, University of Texas Health Science Center at San Antonio, TX

Other Experience and Professional Memberships

2010	Reviewer, Translational Oncology Study Section, NIH/NCI
2011	Reviewer, Netherlands Organization for Scientific Research
2012	Special Emphasis Panel, National Institute of Environmental Health Sciences
2012	Reviewer, North Carolina Biotechnology Center, Collaborative Funding Grant
2012	Reviewer, New York CAP Research Alliance
2012	Program Committee Chair, International Society for Computational Biology (12' ISCB-Asia).
2013-2014	Publications Chair, Great Lake Bioinformatics Conference (13'GLBIO)
2013-2017	Reviewer, NIAID P01/U19/R01 Special Emphasis Panel
2015	Conference Chair, International Conference on Intelligent Biology and Medicine (ICIBM'14)
2015-present	Ad hoc Reviewer (ongoing), GCAT Review Panel, Center for Scientific Review (CSR)
2016-2017	Reviewer, NCI U54/U01 Cancer Systems Biology Special Emphasis Panel
1997-2000	Member, Canadian Chemical Society
2004-present	Member, International Society for Computational Biology
2011-present	Associate Editor, BMC Medical Genetics
2012-2013	Editorial Board, Genomics, Proteomics and Bioinformatics
2013,2015	Guest Editor, BMC Genomics
2017	Guest Editor, Special Issue at Genes

Awards and Honors

1999-2000	Graduate Fellowship, Queen's University, Ontario, Canada
2000-2001	Provincial Graduate Scholarship, Ontario, Canada
2003-2004	"Up On the Roof" Post-doctoral Fellowship, HCG, The Ohio State University, Columbus, OH
2006	Conference Travel Fellowship – ISMB (International Society for Computational Biology) 2006, Brazil
2008	Travel Enrichment Fund, College of Arts & Science, The University of Memphis, Memphis, TN
2012	PhRMA foundation researcher award, presented in ISMB'12, Long Beach, CA
2015	Outstanding Service Award for ICIBM Society

C. Contribution to Science

The major accomplishments in my lab are that we have identified and characterized genomic regulatory elements and networks in various cancer cells through computational modeling and integrating multi-omics-seq data such as ChIP-seq, ChIP-exo, MBDCap-seq, DRIP-seq, TCC/Hi-C, RNA-seq and miRNA-seq. Many of these predictions have been further functionally validated using novel experimental techniques such as CRISPR/Cas9, siRNA, 3C/ChIP/RT-qPCR, Western Blotting, 3D-FISH. Our investigation will not only fundamentally contribute to the understanding of genome/chromatin organization, alternative splicing as well as epigenetic regulation mechanisms, but also provide new approaches to the treatment of cancers. In addition, we have been utilizing our tools as well as others to aid molecular biomarker discovery and further to examine the significance of identified gene signatures in patients' survival and prognostic information.

Omics analyses of one-dimensional (1D) and three-dimensional (3D) transcriptional regulation. We have developed machine learning algorithms and statistical methods for Hi-C and TCC high throughput data. These tools and approaches have been applied in various 'omics-seq data and the predictions have been further experimentally validated.

- a. Lan X, Witt H, Katsumura K, Ye Z, Wang Q, Bresnick EH, Farnham PJ* and **Jin VX***. Integration of Hi-C and ChIP-seq data reveals the distinct types of transcriptional chromatin linkages. *Nucleic Acids Res* 40:7690-7704, 2012. PMCID: PMC3439894.
- b. Hsu PY, Hsu HK, Lan X, Juan L, Yan P, Labanowska J, Heerema N, Hsiao TH, Chiu YC, Chen Y, Liu Y, Li L, Li R, Thompson, IM, Nephew KP, Sharp ZD, Kirma NB, **Jin VX**, and Huang TH. Amplification of distant estrogen response elements deregulates target genes associated with tamoxifen resistance in breast cancer. *Cancer Cell* 24:197-212, 2013. PMCID: PMC3890247.

Computational modeling and functional interrogation on paired-end ChIP-exo data. We have developed novel computational method to process paired-end ChIP-exo data. These methods have been applied in different cell systems and experimentally validated.

- a. Chen Z, Lan X, Thomas-Ahner JM, Wu D, Liu X, Ye Z, Wang L, Sunkel B, Grenade C, Chen J, Zynger DL, Yan PS, Nephew KP, Huang TH, Lin S, Clinton SK, Li W, **Jin VX**, and Wang Q. Agonist and Antagonist Switch DNA Motifs Recognized by Human Androgen Receptor in Prostate Cancer. *EMBO J.*, 34:502-16, 2015. PMCID: PMC4331004.
- b. Chen Z, Lan X, Wu D, Sunkel B, Ye Z, Huang J, Liu Z, Clinton SK, **Jin VX**, and Wang, Q. Ligand-dependent genomic function of glucocorticoid receptor in triple negative breast cancer. *Nature Communications*, 6:8323, 2015. PMCID: PMC4573460.
- c. Ye Z, Chen Z, Sunkel B, Fietze S, Huang TH, Wang Q*, **Jin VX***. Genome-wide analysis reveals positional-nucleosome-oriented binding pattern of pioneer factor FOXA1. *Nucleic Acids Res* 44:7540-7554, 2016. PMCID: PMC5027512.

Deciphering regulatory codes and inferring hierarchal regulatory networks. We have developed machine learning algorithms and statistical methods for discovering *cis*-regulatory modules and *de novo* motifs and reconstructing hierarchal regulatory networks.

- a. ChIPModules: a computational approach utilizing a CART model and comparative genomics information for the identification and characterization of genomic regulatory elements and networks. **Jin VX**, Rabinovich A, Squazzo SL, Green R, Farnham PJ. A computational genomics approach to identify *cis*-regulatory modules for chromatin immunoprecipitation microarray data – a case study using E2F1 in cancers. *Genome Res* 16:1585-1595, 2006. PMCID: PMC1665642.
- b. ChIPMotifs and W-ChIPMotifs: a computational algorithm with a web application tool for *de novo* motif discovery. **Jin VX**, O'Geen H, Iyengar S, Green R, Farnham PJ. Identification of an OCT4 and SRY regulatory module using integrated computational and experimental genomics approaches. *Genome Res* 17:807-817, 2007 (ENCODE issue). PMCID: PMC1891340.
Jin VX, Apostolos J, Nagisetty NSVR, Farnham PJ. W-ChIPMotifs: a web application tool for *de novo* motif discovery from ChIP-based high throughput data. *Bioinformatics* 25:3191-3193, 2009. PMCID: PMC2778340.
- c. Transcriptional Regulatory networks: several approaches have been developed to decipher the regulatory networks. Hierarchical Modularity in ER α Transcriptional Network Is Associated with Distinct Functions and Implicates Clinical Outcomes. Tang B, Hsu HK, Hsu PY, Bonneville R, Chen SS, Huang TH and **Jin VX***. *Scientific Reports* 2:875, 2012. PMCID: PMC3500769.

Dissecting epigenetic-regulated alternative splicing through machine learning algorithms and statistical methods. GESS: a computational model to identify exon-skipping events from RNA-seq data.

- a. Ye Z, Chen Z, Lan X, Hara S, Sunkel B, Huang TH, Elnitski L, Wang Q*, and **Jin VX***. Computational analysis reveals a correlation of exon-skipping events with splicing, transcription and epigenetic factors. *Nucleic Acids Res* 42:2856-69, 2014. PMCID: PMC3950716.

Developing or applying computational pipelines to aid molecular biomarker discovery.

- a. Through computational analysis of miRNA-seq data on a cohort of lung cancer patients, we found miR-31 is able to predict lung metastases. Meng W, Ye Z, Cui R, Perry J, Dedousi-Huebner V, Huebner A, Wang Y, Li B, Volinia S, Nakanishi H, Kim T, Suh SS, Ayers LW, Ross P, Croce CM, Chakravarti A, **Jin VX***, and Lautenschlaeger T* MicroRNA-31 predicts the presence of lymph node metastases and

survival in lung adenocarcinoma patients. *Clinical Cancer Research* 19:5423-33, 2013. PMCID: PMC3823052.

- b. Through computational analysis of MBD-seq data on a cohort of breast cancer patients, we found MT-1 gene cluster can be potential prognostic markers of breast cancer. Jadhav RR, Ye Z, Huang RL, Liu J, Kirma KB, Huang TH*, **Jin VX***. Genome-wide DNA methylation analysis reveals estrogen-mediated epigenetic repression of metallothionein-1 gene cluster in breast cancer. *Clin Epigenetics* 7:13, 2015. PMCID: PMC4355986.
- c. Methyl-binding DNA capture Sequencing for Patient Tissues. Jadhav RR, Wang YV, Hsu YT, Liu J, Garcia D, Lai Z, Huang TH, **Jin VX***. *J Vis Exp*. 31:116, 2016. PMID: 27842364.
- d. Roles of Distal and Genic Methylation in the Development of Prostate Tumorigenesis Revealed by Genome-wide DNA Methylation Analysis. Wang Y, Jadhav RR, Liu J, Wilson D, Chen Y, Thompson IM, Troyer DA, Hernandez J, Shi H, Leach RJ, Huang TH, **Jin VX***. *Sci Rep*. 29;6:22051, 2016. PMID: 26924343.

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1daNr5JAko95k/bibliography/47333145/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

R01 GM114142	Jin (contact PI)	04/13/2015-1/31/2019
NIH/NIGMS		

Omics Analysis of Three-Dimensional Transcriptional Regulation

The goal is to develop computational approaches to dissect three-dimensional transcriptional regulation. We will use the estrogen receptor α (ER α) upon estrogen (E2)-treatment in MCF7 at five time points as a model system (named ER-omics) to study the regulatory role of E2/ER α in breast cancer.

Role: PI

R01 CA172279	Huang (PI)	09/01/2014-06/30/2019
NIH/NCI		

Novel Epigenetic Paradigm in Endometrial Cancer Recurrence

The project's goals are to validate potential epigenetic markers, termed hypomethylators, and investigate their regulatory networks associated with epidermal growth factor receptor (EGFR) and epithelial adhesion marker (EpCAM) during tumor progression.

Role: Co-I

RP150600	Huang (PI)	06/01/2015 - 05/31/2020
CPRIT		

Single-cell Genomic Characterization Core (SGCC) at UTHSCSA

The overall goal of the SBCC is to become an integral part of the CTRC Shared Resources infrastructure. The SBCC is organized into three modules. The PI oversees integration of all modules, each of which is supervised by a module leader who is an expert in the respective research area. The four objectives of the SBCC are to provide: 1) clinical sample processing for single-cell isolation and banking; 2) high-throughput platforms for single-cell identification and characterization; 3) robust single cell based informatics and statistical analyses for data integration and interpretation; and 4) outreach and pilot project programs to enhance the SBCC user base, seed collaborations and support early stage investigators.

Role: Co-I

R01CA193835	Sharp (PI)	12/01/2015 – 11/30/2020
Delaying intestinal cancer		

The overall goal of this proposal is to use intestine cancer as a model to test the general proposition that long-term mTORC1 inhibition extends life span (and health span) by delaying cancer.

Role: Co-I

PC150382	Wang (PI)	08/01/2016 – 07/31/2019
DOD		

Novel Tumor Suppressive Role of Phosphodiesterases in Prostate Cancer

The overall goal of this project is to test the hypothesis that Phosphodiesterase inhibitors (PDEs) exhibit tumor suppressive functions as negative regulators of prostate cancer relevant oncogenic signaling pathways.

Role: Co-I

RP170126

Hu (PI)

12/01/2016 – 11/30/2019

Novel Pathway to Reduce BRCA1-Associated Breast Cancer Risk

The overall goal of this proposal is to combine mouse genetics, functional genomics and comparative analyses of clinical samples to understand the roles of BRCA1 in the tissue-specific tumor suppression.

Role: Co-I

Completed Research Support

R21 HG006761

Farnham (PI)

04/01/2012 -- 03/31/2015

NIH/NHGRI

Development of a Nuclease-Mediated technology to Validate Chromatin Hubs

The goal of this study is to develop a nuclease-mediated technology to validate chromatin hubs in the human genome predicted from computational approaches.

Role: Co-I

P01 CA097189

Ostrowski (PI)

07/01/2012 -- 08/30/2016

NCI/NIH

Genetic Analysis of the Breast Tumor Microenvironment

The goal of this proposal is to study the genetic changes for the breast tumor microenvironment in pre-clinical models.

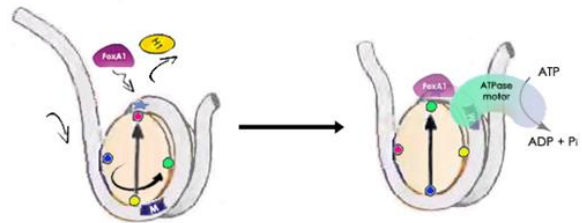
Role: Co-I

Title: Pioneer factor mediating epigenetic control of prostate cancer progression

Many studies, including ours, have found both FOXA1 and GATA2 act as pioneer factors (PFs) to trigger androgen receptor (AR) signaling pathway for hormone circulation in prostate cancer (PCa) cells. These PFs can recruit various enzymes such as chromatin modifiers and chromatin remodelers to establish an "open" chromatin environment or a nucleosome-free region (NFR) to facilitate the accessibility for other transcription factors (TFs), then to initiate subsequent regulatory events. However, how the underlying nucleosome is destabilized and how the PFs locate their targets amidst the tangle of nuclear chromatin remains elucidated. Although ChIP-seq enables us to map in vivo TF binding and histone modifications in a genome-wide manner, the length of binding sites identified from ChIP-seq data by different computational tools usually varies from 300-500 bp which is much wider than an actual length of the canonical TF binding motif. The very recent ChIP-exo technique developed in the Pugh Lab modified a key step of ChIP-seq protocol by using of lambda exonuclease digestion and now allowed identification of a TF binding location at single nucleotide resolution. Our recent work used a modified strand-specific paired-end ChIP-exo, termed here as ChIP-ePENS, to reveal four distinct modes of border-composed sites (BCSs) for FOXA1 and GATA2 in LNCaP cells, providing an underlying structural and mechanistic insight into the dynamics of a positional-nucleosome-oriented PF binding pattern. In this project, we plan to determine the combinatorial pattern of remodelers and histone modifications associated with BCSs in a prostate cancer cell system. Through such a comprehensive data analysis, much detailed structural roles of FOXA1 and GATA2 and their interplay with nucleosome particles may be elucidated.

Hypothesis

Based on our previous studies and preliminary data, we hypothesize that FOXA1 and/or GATA2 may compete with linker H1 and coordinate with chromatin remodeling complexes to dynamically regulate the nucleosome positioning and spacing, and further to govern prostate cancer progression (Fig 1. right).



Project Aims and Approaches

Aim 1: Conduct omics-seq data in a prostate cancer cell system. We will generate different omics-seq profiling, including ChIP-ePENS of FOXA1, GATA2, AR, ChIP-seq of H1, MNase-ChIP-seq of H3, various remodelers, H3K4me1/3, H3K27ac and H3K27me3, H3K9me3, and RNA-seq at the DHT-treated or vehicle conditions in normal prostatic epithelial cells (PWR-1E) and PCa cell lines, LNCaP, LNCaP-abl, C4-2B and PC3. Each sample will be conducted in biologically duplicates with ~30 million reads/replicate. The data quality will be carefully controlled by ENCODE guideline.

Aim 2: Test the hypothesis on a prostate cancer cell model system and perform mechanistic and functional validations. We will apply ePEST to precisely define cell-specific FOXA1/GATA2-mediated border-composed binding patterns. We will estimate nucleosome positioning and spacing to identify combinatorial nucleosomal patterns (particularly remodelers) associated with cell type-specific FOXA1/GATA2 regulated BCSs respectively. To elucidate their mechanistic and functional roles, we will use CRISPR-cas9 to edit out one or two cell-specific remodelers (csRM) in each of three AR+ PCa cells to create ΔcsRM sublines respectively. We will select 3-5 FOXA1, GATA2 or FOXA1/GATA2 mediated binding loci (genes) relevant to prostate cancer progression to conduct: 1) ChIP/RT-qPCR to examine the changes of binding levels of FOXA1/GATA2/AR, histone marks, other RMs and of expression levels by comparing parental vs ΔcsRM at DHT-treated vs vehicle conditions respectively, and further to identify the determinants of regulating nucleosome positioning and spacing; and 2) cell proliferation and invasion assays to assess their oncogenic potential (or transformed phenotype).

Our integrative approaches may provide new insights into the structural, mechanistic and functional relationship among nucleosome positioning and spacing, FOXA1, GATA2 and AR, revealing how they govern androgen-dependent prostate cancer development and progression.